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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/934,249	08/21/2001	Richard T. Lee	P0738/7001 (ERP/KA)	6506

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 08/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/934,249	LEE ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-11,68,80-83 and 86-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-11,68,80-83 and 86-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Currently claims 1-4, 8-11, 68, 80-83, and 86-90 are pending and under consideration in the application. Claims 1-4, 8-11, 68, 80-83, and 86-88 were rejected in the prior action, mailed on April 7, 2005. In the Response filed on July 7, 2005, the Applicant amended claims 1, 4, 10, 11, and 89.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. **(Prior Rejection- Withdrawn)** Claims 1-4, 8-11, 68, 80-83, 86-90 were rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The claims were rejected as lacking a specific and substantial utility because the Applicant has provided no evidence tying the expression of the protein designated MIVR-1 with any heart related disease or disorder. In view of Applicant's assertion of a anti-apoptotic activity, the utility rejection is withdrawn.

4. **(Prior Rejection- Withdrawn)** Claims 10 and 11 were rejected under 35 U.S.C. 101 because the claims read on a human being, which is not patentable subject matter. In view of the amendment of the claims to read on "isolated" host cells, the rejection is withdrawn.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. **(Prior Rejection- Maintained)** Claims 1-4, 8-11, 68, 80-83, 86-90 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims were rejected because the application does not enable those in the art to practice the claimed invention as the application does not teach what disorders may be diagnosed using the claimed nucleic acids, or the encoded peptides.

The Applicant traverses the rejection on the grounds that that the protein has been shown to be up-regulated in response to strain, which the Applicant asserts is recognized by those in the art to be a hypertrophic agonist (citing the Keulenaer reference in support), which demonstrates the protein's use as a diagnostic marker for hypertrophic disorders. These arguments are not found persuasive.

With respect to the diagnostic potential of the MIVR-1 protein, the Applicant notes its production in cardiac cells under strain, and concludes that because strain is recognized by those in the art to be a hypertrophic agonist, the expression of the protein must correlate with a disease condition associated with hypertrophy. In support of this assertion, the Applicant points generally to the teachings of Keulenaer et al., (Circ Res 90: 690-96). However, this reference

does not support the Applicant's conclusions that 1) strain is in itself indicative of a disease condition, or that 2) any protein induced by such strain is a marker for a hypertrophic condition. Rather, the reference teaches that proteins and pathways induced by strain may lead either to adaptive hypertrophic growth (a positive outcome), or to the regulation of cell death and heart failure. Page 690. With respect to these different pathways, the Keulenaer reference specifically states "The detailed molecular biology and the downstream genes activated by these signaling pathways, however, are incompletely understood." Page 690. This reference therefore teaches that strain may lead to disease conditions, but that such is not necessarily true, and further that those in the art are not knowledgeable as to what pathways or proteins lead to what outcomes.

In addition to these teachings of uncertainty and limited knowledge in the art, as was indicated in the prior action, the art does recognize that mechanical strain is in inherent feature of cardiac cells. See e.g., U.S. 2002/0072674, (cited on page 5 of the prior action). These teachings implicitly recognize that the mere presence of strain in cardiac cells is not in itself indicative of a disease condition. Thus, the teachings of the art indicate that the presence of strain is a general feature of heart cells.

The teachings of both of these references are further supported by the teachings of Feng et al., Circ Res 85: 1118-1123 (cited in the IDS of Jan 2003). This reference both recognizes that smooth muscle cells of the arteries residues in mechanically active environments. Page 1122. The reference additionally identifies genes up-regulated in response to the strain, included among them a gene identified as PAI-1, which reference teaches was up-regulated in mechanically strained vascular smooth muscle cells. However, the reference teaches that the short and long term effects of the protein were uncertain even given that, unlike in the present

application with respect to MIVR-1, the reference did have additional experimental evidence of the proteins activities. Id. In short, the reference supports the Examiner's position that the teachings in the current application provide insufficient information to enable those in the art to determine that the MIVR-1 protein would be useful as a marker of heart disease because there are insufficient teachings relating to its activities in the cells.

In view of these teachings, and the lack of specific teachings associating the MIVR-1 protein to any specific disease condition, or even linking this specific protein to any specific function or functional pathway in cardiac cells, the rejection is maintained.

7. **(Prior Rejection- Withdrawn)** Claims 10 and 11 were rejected under 35 U.S.C. 112, first paragraph, as because the specification is not enabling for host cells comprised within either the human patient or the transgenic animal. In view of the amendment of these claims to read on "isolated" host cells, the rejection is withdrawn.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. **(Prior Rejection- Maintained)** Claims 1, 4, 68, 81, 88, and 89 were rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al., Genomics 66: 257-63 (of record in the January 2003). The Applicant has amended the claims to require that fragments according to subpart (b) of the claim have a sequence of at least 23 nucleotide. However, the Applicant has not required more than 22 nucleotides in subpart (a), which reads on probes to SEQ ID NO: 1, which includes SEQ ID NO: 3. Thus, any probe to SEQ ID NO: 3 would also be a probe to SEQ ID NO: 1. Because Xu teaches a probe of SEQ ID NO: 3, and therefore of SEQ ID NO: 1, comprising 22 bases, the rejection is maintained with respect to claims 1, 4, 68, 81, and 88. However, because claim 89 has been amended to read on only nucleotides of at least 24 bases, the rejection is withdrawn from this claim.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. **(New Rejection- Necessitated by Amendment)** Claims 1, 4, 68, 81, 88, and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu as applied to claims 1, 4, 68, 81, and 88 above, and further in view of the teachings of Kumar (U.S. 5,916,776) and Buck et al. (BioTechniques 27: 528-36). The teachings of Xu have been described previously in part. As indicated in the prior action, the reference teaches the making and use of probes and primers for

the detection of an identified gene. However, while the reference teaches primers of 20 and 22 bases that hybridize to SEQ ID NO: 3 or its complement (and therefore to SEQ ID NO: 1 or its complement) the reference does not teach primers of greater length.

However, the Kumar reference teaches that probes and primers may comprise anywhere from 15 to 500 nucleotides. See e.g., column 18, lines 26-42. It would therefore have been obvious to those of skill in the art to use primers of any of these lengths that comprise the sequence of the gene disclosed on page 259 of the Xu reference, or complements thereto. Those of skill in the art would have had a reasonable expectation of success in the use of such probes or primers based on the teachings of Kumar indicating that sequences of any of these lengths may be used. The teachings of Buck et al., indicating that the actually sequence of a probe or primer is not important provides additional grounds for those of ordinary skill in the art to expect that any probe or primer would be effective. Thus, the combined teachings of these references render the claimed inventions obvious.

Conclusion

12. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 8/19/05

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